Please add new claims 34 and 35:

--34. (New) The protein of claim 1 comprising the amino acid sequence of sequence ID No. 2.--

a3

--35. (New) A polypeptide fragment of claim 34, wherein the fragment comprises amino acid 297 to amino acid 567.--

II. REMARKS

Claims 1 to 33 are pending in the subject application. Claims 6 to 21 and 22 to 23 (non-protein species) have been withdrawn from consideration as the result of a requirement for restriction. By this Amendment, these claims have now been canceled without prejudice to Applicant's right to pursue prosecution of these claims in a later filed continuation or divisional application. The cancellation of these claims and the addition of new claims 34 and 35 are not intended to be a dedication to the public of the subject matter of the originally filed claims.

The specification has been amended to correct typographical and grammatical errors. Claims 1 and 22 have been amended to remove the language "having the ability" as suggested by the Examiner. Claim 1 also is amended to more clearly point out and distinctly claim the subject matter of the invention. The term "mammalian CD40 receptor" has been added to indicate that the mammalian protein binds its mammalian receptor. The claim element "but does not bind a homologous cell surface receptor of the tumor necrosis family" is supported on page 1, lines 15 to 28 and on page 30, line 30 to page 31, line 27. Claim 2 has been amended to insert the element "comprising the C-terminal half". Support for the amendment is found in the specification on page 37, lines 30-33. New claims 34 and 35 are supported in the application papers on pages 7, 37 and sequence ID No. 2. The claims also have been renumbered since a

claim numbered "22" was missing from the claims as filed. No new matter is introduced by these amendments and entry thereof is respectfully requested. Claims 1 to 5, 22 and 23 (protein species) and new claims 34 and 35 are presently under examination.

In view of the preceding amendments and remarks, reconsideration and withdrawal of the objections and rejections set forth in the outstanding Office Action are respectfully requested.

Requirement for Restriction

The claims were subject to a restriction requirement under 35 U.S.C. § 121 to one of the following allegedly independent and distinct inventions:

I. Claims 1 to 5, 22 and 23, drawn to a purified mammalian protein, a polypeptide fragment, compositions and agents that inhibit binding to the cytoplasmic domain of CD40 receptor;

II. Claims 6 to 17 and 28, drawn to an isolated nucleic acid molecule, expression vector, a host vector system encoding CD40bp, and a method of producing the protein or polypeptide;

III. Claims 18 to 27, drawn to antibodies, agents that are anti-CD40 antibodies, antibody fragments, and hybridoma cell lines;

IV. Claims 29 to 31, drawn to a method of modulating cellular functions by transfecting cells with nucleic acids encoding CD40 binding proteins; and

V. Claims 32 and 33, drawn to a method for screening for a CD40 immunosuppressive agent.

On March 7, 1996, a provisional election, with traverse, was made to prosecute the invention of Group I, claims 1 to 5, 22 and 23. The election is affirmed.

Objections to the Specification

The Examiner pointed out and required correction of typographical and grammatical errors and renumbering of the claims. In view of the corrections made herein, removal of the objections to the specification is respectfully requested.

35 U.S.C. § 112, First Paragraph

Claims 1 to 5, 22 and 23 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly not being enabled by the specification. The Office states that the specification describes CD40 binding protein as a protein putatively involved in the signal transduction of the CD40 receptor as the protein binds to the cytoplasmic domain of the CD40 receptor. In brief, it is alleged that the specification fails to set forth sufficient physical and functional characteristics to support breadth of the claims. For example, the element "mammalian" appearing in the claims is allegedly not enabled since the specification does not state that the gene is conserved between all mammalian species. The specification also is alleged to provide insufficient working examples to enable all fragments from all 64kd proteins having the ability to bind to the cytoplasmic domain of CD40.

For the reasons provided below, Applicant traverses.

Claims 1 and 2 have been amended to more clearly define the scope of Applicant's invention. The amendment to claim 1 more clearly defines that the purified protein of Applicant's invention specifically binds to the CD40 receptor, but not a homologous cell surface receptor of the tumor necrosis family. Based on sequence information (e.g. Seq. ID No.2) an amino acid analysis revealed a RING finger domain and coiled-coil domains. In Experiment I appearing in the specification, CD40 was cotransformed with: native CD40 or heterologous baits of mutant CD40, the cytoplasmic domain of the p55 TNF receptor, FAS receptor, truncated p55 TNF receptor, the helix-loop-helix motif of E12 and the yeast Ser-Thr kinase SNF1. Colonies

from each transformation were patched onto a selective plates. As shown in Figure 1, CD40bp interacted with native CD40 only. It did not interact with mutant CD40 or the other baits of receptors from the tumor necrosis family, showing that the CD40-CD40bp interaction was specific as measured by the yeast cotransformation assay.

With respect to the generation of a variety of fragments of CD40bp, Applicant has identified that the C-terminus is required for binding to CD40 and provided a simple in vitro screen for CD40 binding. Applicant also has provided in one embodiment, the full amino acid sequence for CD40bp. This information fully enables the claim to polypeptide fragments because, one of skill in the art, using Applicant's disclosure, can make numerous fragments and assay for CD40 binding specificity. Indeed, other investigators have made such polypeptide fragments that fall within the scope of Applicant's claims (see prior art cited against the claims, below).

With respect to the term "mammalian", one of skill in the art need not teach, and preferably omits, what is well known to those of skill in the art. Hybritech v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). It was known prior to Applicant's invention that CD40 is present on various mammalian cells and therefore, an intracellular ligand must be present. However, it was not until Applicant's invention that the intracellular ligand as well as its cDNA, and amino acid sequence, were deduced. Therefore, with this information in hand, it would not require an undue amount of experimentation for one of ordinary skill in the art to isolate, clone, and sequence the homologous intracellular protein in another mammalian species, for example, in a mouse cell. Indeed, after the reduction to practice of the subject invention, other investigators isolated the

homologous protein in murine cells (Cheng, et al. Science (1995) 267:1494 at page 1495, column 3).[1]

With respect to claims 22 and 23, page 7, lines 3 to 13, provides examples of several embodiments falling within the claims. It is well within the skill of the ordinary artisan, having the sequence as well as the isolation procedures provided in Applicant's disclosure, to make and screen antibodies having the ability to inhibit the binding of CD40bp to CD40. Indeed, it has been held that the screening of antibodies for a defined specificity is not "undue experimentation" within the meaning of 35 U.S.C. § 112, first paragraph. In re Wands, 858 F.2d 731 (Fed. Cir. 1988).

Specifically with respect to claim 23, the plain language of the claim provides the meets and bounds of the claim to "a dominant inhibitory fragment". It is, as the claim indicates, an agent (such as a fragment of CD40bp) that inhibits the binding of CD40bp to the intracellular domain of CD40. The knowledge and skill in the art at the time the application was filed, in addition to the in vitro binding assay provided in the specification, fully enables the claim.

In view of the preceding amendments and remarks, reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 112, first paragraph, are respectfully requested.

35 U.S.C. § 112, Second Paragraph

Claims 1 and 5, 22 and 23 stand rejected under 35 U.S.C § 112, second paragraph, for allegedly being indefinite and for allegedly failing to particularly point out and distinctly claim the subject matter thereof. The Examiner objected to the claim language "having the ability to". This language has been removed from the pending claims. Removal of the rejection is respectfully requested.

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[1] In the Note added in proof section of the paper, the authors of Cheng et al. acknowledge that the protein identified and described therein is the same as Applicant's previously reported protein (reference 32 of the Cheng et al. paper).

35 U.S.C. § 102

Claims 1 to 5 and 22 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Hu et al., Sato et al., Cheng et al. or Mosialos et al.

Hu et al. is Applicant's own publication and thus, cannot be used as prior art against the claimed invention under 35 U.S.C. § 102 or § 103. In support of the position that the publication is Applicant's own, attached hereto is an "In re Katz" declaration under 37 C.F.R. § 1.132. In view of this declaration, removal of the rejection of the claims over Hu et al. is respectfully requested.

Applicant also submits herewith a declaration under 37 C.F.R. § 1.132 showing a conception and reduction to practice of the invention prior to the publication of Sato et al., Mosialos et al. and Cheng et al. In view of the submission of this declaration, removal of the rejection of the rejection of the claims as allegedly anticipated by these references is respectfully requested.

III. CONCLUSION

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952 (Our Ref. 20344-21025.00)**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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